THE EFFECT OF THE DOUBLE BOND ON THE REACTIVITY OF ORGANIC COMPOUNDS.

By

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Submitted to the Department of Chemistry and the Faculty of the Graduate School of the University of Kansas in partial fulfillment of the requirements for the degree of MASTER OF ARTS.

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June, 1925.

The work outlined in this paper was conducted under the direction of Dr. F. B. Dains. I am very grateful to him for his assistance and supervision.

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INTRODUCTION.

The object of this work was to study reactions involving the breaking of carbon to carbon double bonds. The study was confined largely to the reactivity of methylene groups in which the hydrogen had been replaced by benzal groups or those of similar character. Diphenyl-formamidine was largely used in the effort to replace the benzal grouping in substituted methylene compounds. Two phases of the problem were investigated. First, it was thought desirable to determine what effect the presence of different groups, adjacent to the methylene group, had on the ease with which the C = C grouping could be broken. Second, several attempts were made to ascertain the influence of the double bond on the reactivity of adjacent keto groups.

The characteristic reactions of the C = C grouping are:

1. They react with nascent hydrogen forming saturated compounds.
2. They add halogen acids, especially HI.
3. Concentrated sulfuric acid absorbs them forming ethereal salts.
4. They form dihalides by addition of Cl_2, Br_2, I_2, and ClI.
5. They yield chlor-hydrins with acqueous HClO.
6. Potassium permanganate in dilute solution

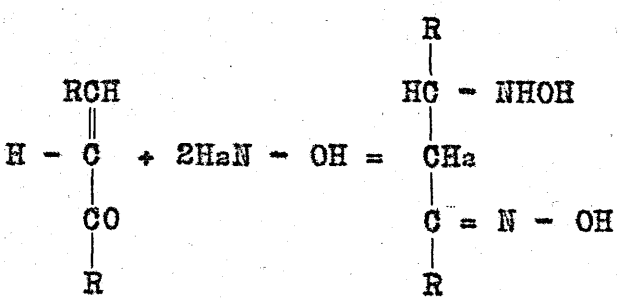
changes them to glycols.

7. More energetic oxidation with potassium permanganate or other strong oxidizing agents breaks the double bond. Ozone will break the bonds and form ozonides[1]. The ozonides are decomposed by H_2O yielding two molecules of aldehydes or ketones. The reaction follows:

$$R_2C = CR'_2 \longrightarrow R_2C \overset{O_3}{\diagdown\diagup} CR'_2 \longrightarrow R_2CO + R'_2CO$$

8. When acted upon by dilute H_2SO_4, $ZnCl_2$, boron fluoride, and many other substances, olefines undergo polymerization even at ordinary temperatures. This is due to the union of several molecules by addition at the double bond.

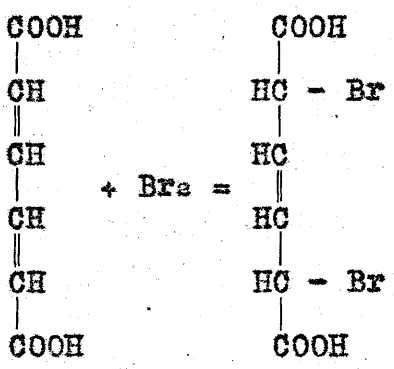
9. The reactivity of the double bond is considerably influenced by the presence of certain groups, notably the CO group. The additive power of the C = C group is greatly increased. Hydroxyl amine reacts with such a double bonded group, as well as with the adjacent CO group. The general reaction follows:



10. Hydrazines react with CO group and with the C = C group forming cyclic pyrazolines.

11. Mercaptans add to both the C = C and CO groups. This reaction occurs even when the two groups are not adjacent.

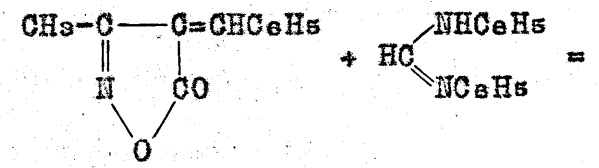
12. When the double bonds are found in the same chain, adjacent respectively to CO groups as in muconic acid, the compound does not add 2 molecules of bromine as might be expected. Muconic acid adds only one molecule of bromine and the double bond shifts to the center. The reaction follows:

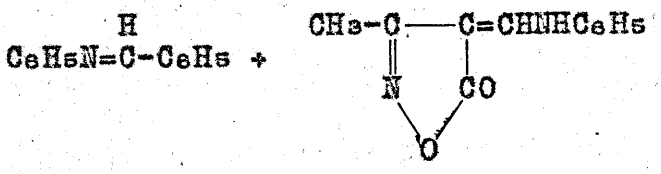


Because of these and similar reactions, Thiele[2] has advanced his theory of partial valences.

The literature does not show that very much work has been done in studying the conditions under which one doubly bound group may be replaced by another. Most of the reactions found in the literature which result in the breaking of double bonds are either oxidation or hydrolysis reactions.

F. B. Dains and Griffin[3] showed that the benzal group might be replaced with the anilido methylene group by treatment with diphenyl-formamidine. The equation for the reaction is:





The formamidine reacts readily with compounds which contain the methylene grouping. These reactions have been extensively studied[4].

The general reaction may be expressed as follows:

$$\text{>CH}_2 + \text{RN=CHNHR} = \text{C=CHNHR} + \text{RNH}_2$$

It was thought desirable to study more fully the conditions under which the benzal grouping could be replaced by the anilido methylene group from diphenyl-formamidine. Efforts were made to see whether the benzal group could be replaced with equal ease when groups other than the CO grouping were adjacent. Attempts were made to get diphenyl formamidine to react with each one of the following substances:

1. Benzal-phenyl-methyl-pyrazolone.

2. Piperonal-phenyl-methyl-pyrazolone.

3. Cinnamyl-phenyl-methyl-pyrazolone.

4. Benzal-diortho-tolyl-thiazolidone.

5. Benzal-phenyl-rhodanine.

6. Cinnamyl-phenyl-rhodanine.

7. Benzal-malonic-ester.

8. Benzal-acetoacetic-ester.

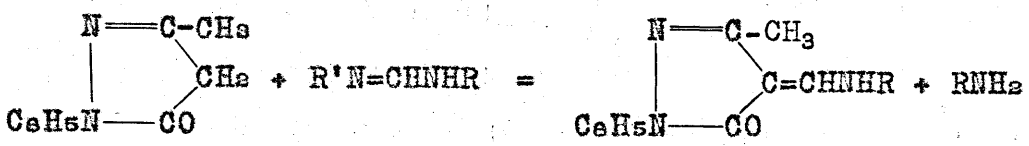
9. Benzal-acetophenone.

In a few cases, the above condensation products were treated with phenyl hydrazine in order to determine whether the aldehyde group could be removed by this reagent. In addition, benzal acetophenone was allowed to react with aniline, para-toluidine and parachloraniline.

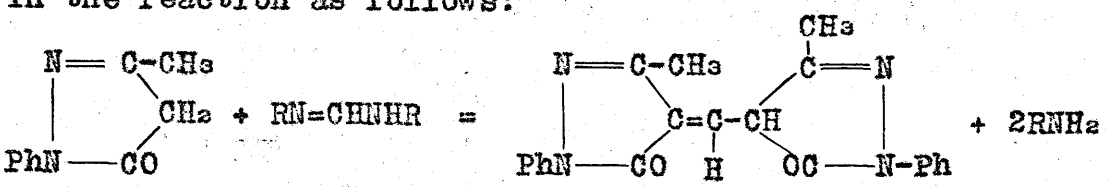
EXPERIMENTAL.

Benzal-Phenyl-Methyl-Pyrazolone with Diphenyl Formamidine.

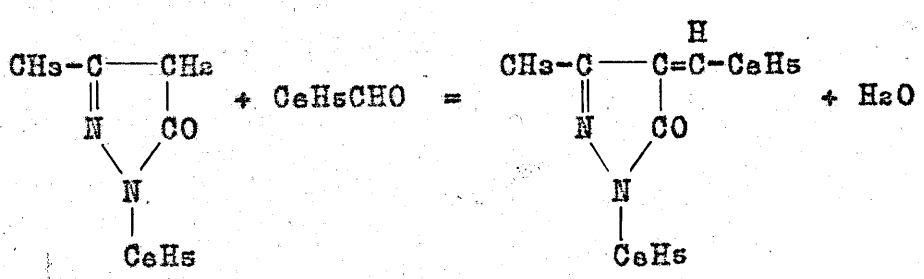
It has been shown that phenyl-methyl-pyrazolone and the formamidines react easily and smoothly according to the following equation:[5]



Methyenyl-bis-methyl-phenyl-pyrazolone is often formed in the reaction as follows:

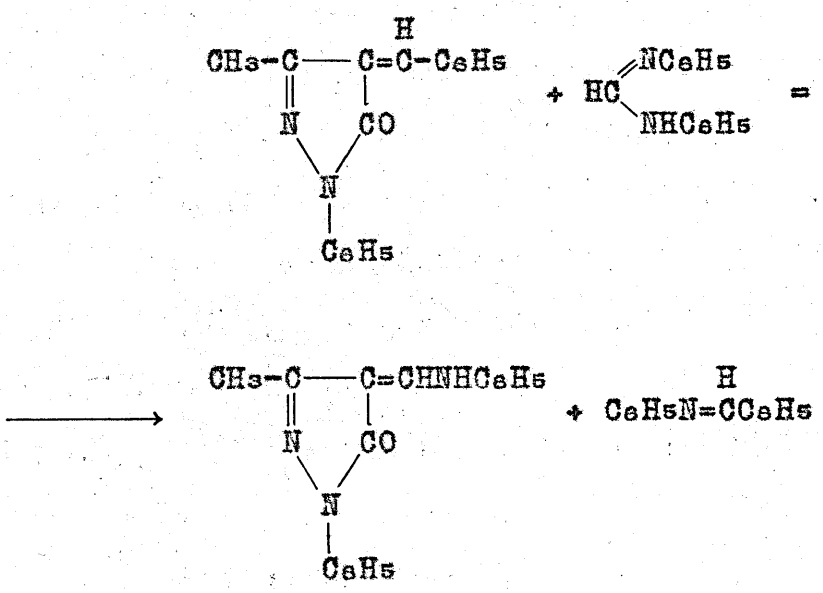


Benzal-phenyl-methyl-pyrazolone was prepared after the method of Korr[6]. Molar proportions of freshly distilled benzaldehyde and phenyl methyl pyrazolone were mixed and heated in an oil bath for thirty minutes at 140°. The condensation takes place easily and without the aid of any condensation agent. On recrystallization from alcohol, a bright red crystalline product was obtained which melted at 107°. The reaction is as follows:



The benzal-phenyl-methyl-pyrazolone was mixed in molar proportions with diphenyl-formamidine and heated in an oil bath for one hour at a temperature of 140°. Fractional crystallization was carried out in benzene. A considerable part of the diphenyl-formamidine was recovered unchanged but after several fractionations a yellow crystalline compound was obtained which melted at 154° . A mixed melting point showed this product to be identical with the one obtained by heating phenyl-methyl-pyrazolone and diphenyl formamidine directly. The yield was about 20%. The above reaction showed that the anilido-methylene grouping from the diphenyl-formamidine would replace the benzal group as in the case of benzal-isoxazolone[7]. The

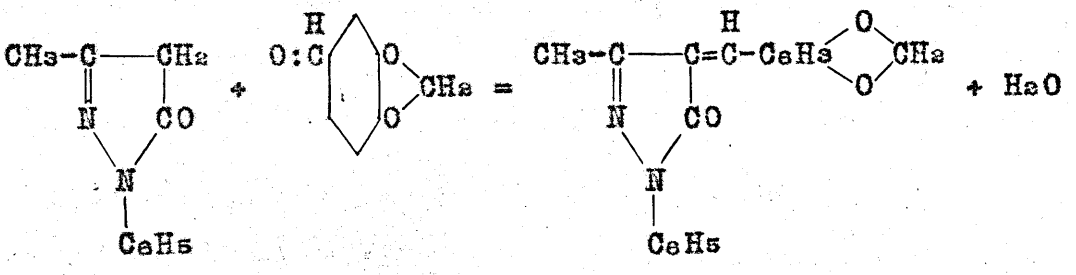
reaction evidently is as follows:



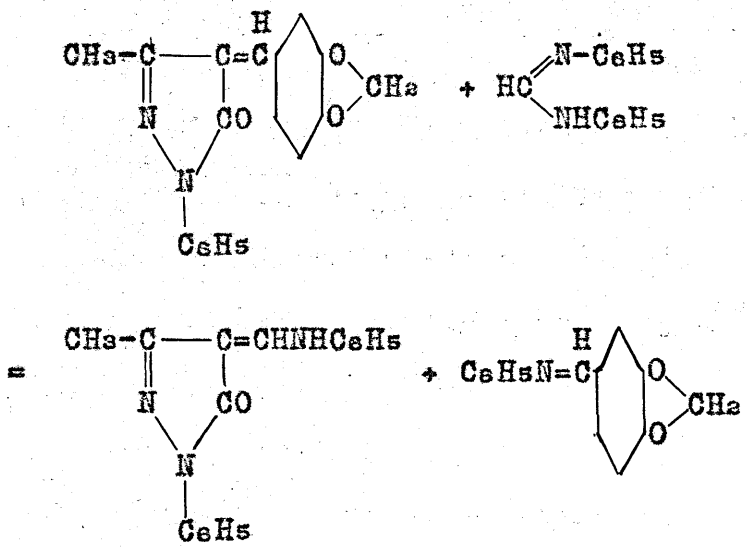
Piperonal-Phenyl-Methyl-Pyrazolone with Diphenyl Formamidine.

In order to determine whether similar aldehyde groups could be removed with equal ease, the piperonal derivative of phenyl-methyl-pyrazolone was tried with diphenyl-formamidine and with phenyl-hydrazine.

Molecular proportions of piperonal and phenyl methyl pyrazolone were mixed and heated after the method of J. Tambor[8]. The condensation is easily accomplished by heating for thirty minutes in an oil bath at a temperature of 140°. A quantitative yield was obtained. The red crystalline mass was crystallized from alcohol. Deep red crystals were obtained which melted at 168°. The reaction is as follows:

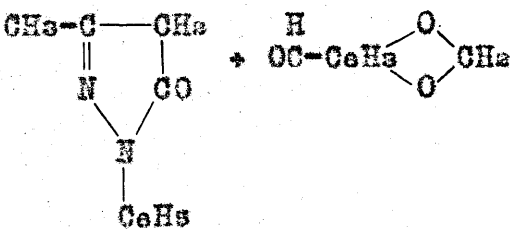


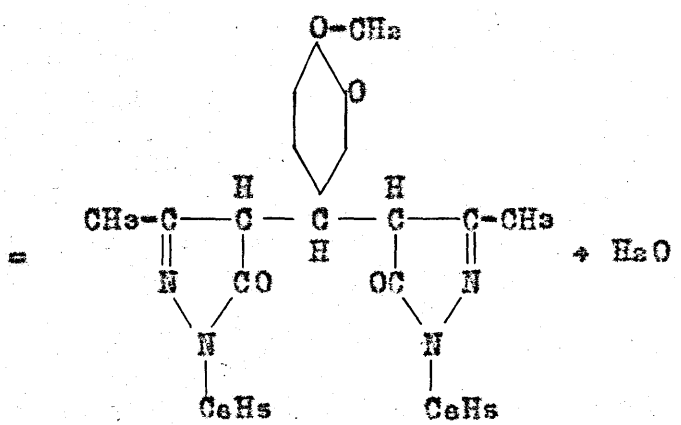
Molar proportions of the above condensation product were mixed with diphenyl-formamidine and heated in an oil bath for thirty minutes at 140°. The mass was dissolved in benzene and allowed to stand several days. The products were separated by several crystallizations from benzene. A yellow product was isolated which crystallized in needles melting at 154°. A mixed melting point showed that this product was identical with the one obtained by treating benzal-phenyl-methyl-pyrazolone with diphenyl-formamidine. The reaction is similar and as follows:



Piperonal-Bis-Phenyl-Methyl-Pyrazolone with Diphenyl Formamidine.

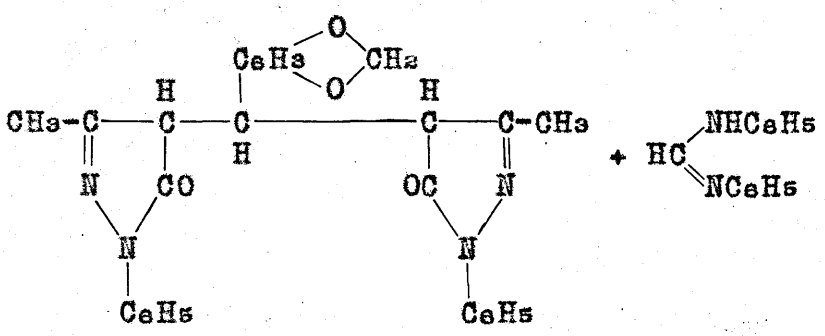
J. Tambor[9] showed that under certain circumstances two moles of phenyl-methyl-pyrazolone would react with one mole of piperonal. His method was followed in the preparation of the condensation product. Two moles of phenyl-methyl-pyrazolone were mixed with one mole of piperonal. The mixture was heated for five minutes at a temperature of 120°. A yellow crystalline mass was obtained. This was recrystallized from 50% alcohol. Nearly white crystals were obtained which melted at 143°. The reaction is as follows:

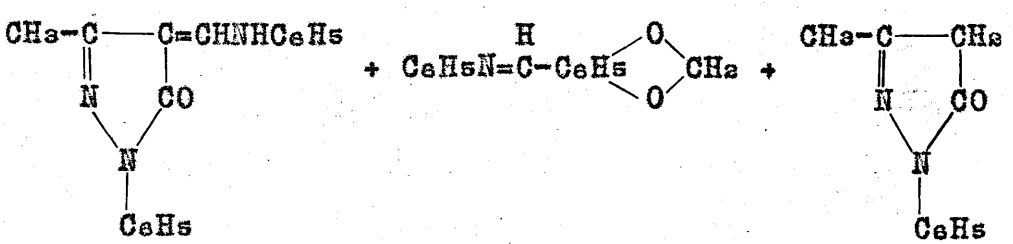




The piperonal-bis-phenyl-methyl-pyrazolone so obtain-

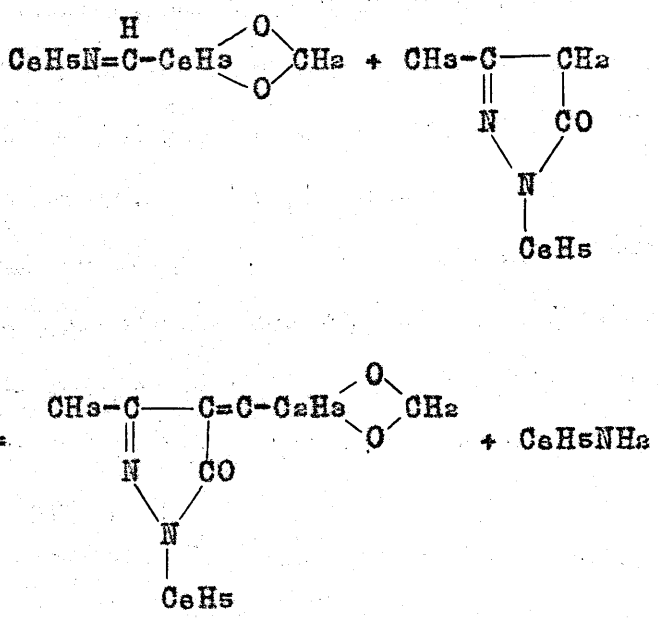
ed was mixed in molar proportions with diphenyl-formamidine and heated for twenty minutes at a temperature of 130°. It was thought that some reaction with diphenyl-formamidine might take place whereby two molecules of pyrazolone might be joined to some part of the diphenyl-formamidine molecule. This did not prove to be the case as far as could be learned. The same annilido-methylene-phenyl-methyl-pyrazolone product was obtained as when the benzal-phenyl-methyl-pyrazolone condensation product was heated with diphenyl formamidine. The reaction probably took place as follows:





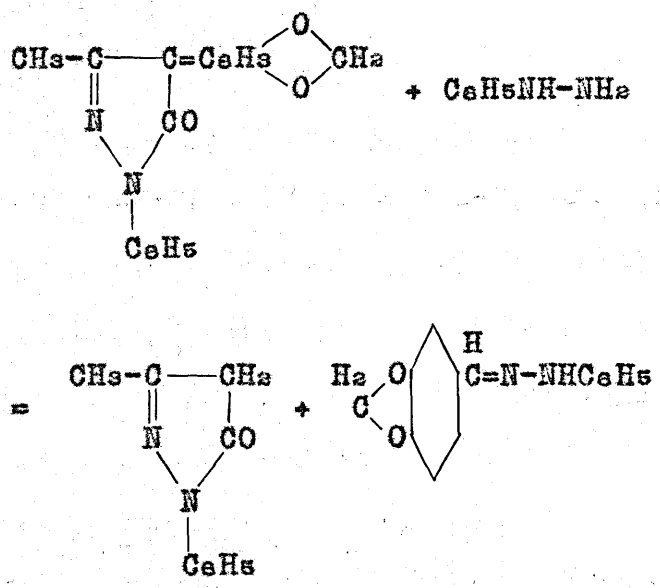
A deep red crystalline substance which melted at 168° was also obtained from the reaction. A mixed melting point showed this to be identical with the regular piperonal-phenyl-methyl-pyrazolone condensation product. Since bleaching powder test showed the presence of aniline, it

was decided that a secondary reaction probably took place as follows:



Piperonal-Phenyl-Methyl-Pyrazolone with Phenyl Hydrazine.

The piperonal pyrazolone condensation product was heated with phenyl hydrazine in alcohol solution. The solution was refluxed for thirty minutes on a water bath. On standing, a substance crystallized from the alcohol which melted at 102°. Piperonal hydrazone was prepared and a mixed melting point showed the reaction product and the hydrazone to be identical. The reaction is similar to that reported by Meyer[10] in the case of certain substituted isoxazolones. It evidently takes place according to the following equation:



As an added argument in favor of the above reaction, the piperonal pyrazolone condensation product was mixed with freshly distilled phenyl hydrazine and the flask was placed for thirty minutes in a bath of boiling water. The mass was then treated with a large volume of boiling water. Small quantities of phenyl-methyl-pyrazolone were extracted and identified by means of a mixed melting point determination.

Cinnamyl-Phenyl-Methyl-Pyrazolone with Diphenyl-Formamidine.

Cinnamic aldehyde and phenyl-methyl-pyrazolone were condensed according to the method of Ludwig and Knorr[11]. Ten grams of phenyl-methyl-pyrazolone and four grams of cinnamic aldehyde were mixed. They react very readily at room temperature producing considerable heat. A deep red condensation product was obtained when heated for an hour at 120°. When crystallized from alcohol, the condensation

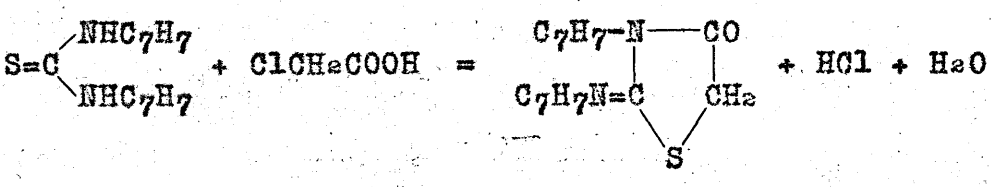
product method at 158°.

Molar quantities of cinnamyl-phenyl-methyl-pyrazolone and diphenyl-formamidine were dissolved in xylol and refluxed for two hours. The xylol was distilled off and an amorphous mass was obtained. Considerable polymerization seemed to have occured for all attempts to obtain a crystalline product from the mass were unsuccessful.

Benzal Di-Ortho-Tolyl-Thiazolidone with Diphenyl-Formamidine.

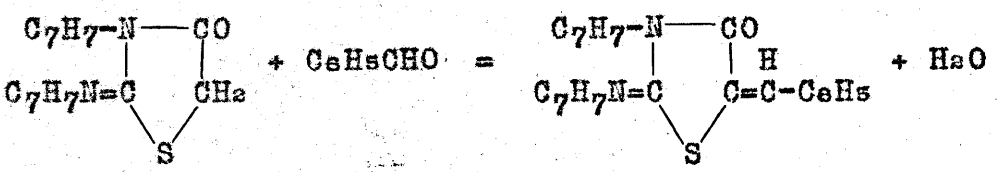
The question of whether the benzal group could be broken with equal ease when sulfur was adjacent to the methylene grouping was next studied. The grouping -CO-CH_2-S has been shown to condense with aldehydes and behaves very much like the CO-CH_2-CO grouping.[12]

The diortho-tolyl-thiazolidone was prepared by heating chlor-acetic acid with diortho-tolyl-thiourea. The reaction is as follows:



Several methods for obtaining the benzal condensation product were tried. It was observed that while benzaldehyde would condense with the thiazolidone, the condensation was not nearly so easily accomplished as in the case of the CO-CH_2-CO grouping. The best yield was obtained by following the method of Wheeler and Jamieson[13]. Twenty-five grams of the di-ortho-tolyl-thiazolidone and eight

grams of freshly distilled benzaldehyde were dissolved in 400 c.c. of absolute alcohol. One and nine-tenths grams of sodium were then added. Mixture was refluxed on a water bath for three hours. The alcohol was then almost completely distilled off. Water and dilute acetic acid were added and the product was washed thoroughly. On recrystallization from alcohol, light yellow crystals were obtained which melted at 178°. The yield was about fifty per cent. The reaction is as follows:

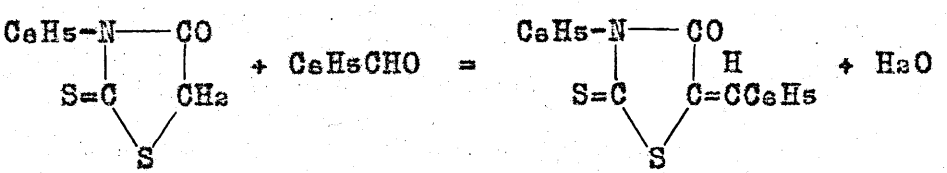


Although numerous attempts were made to replace the benzal group in the above condensation product, all trials were failures. Molar proportions of diphenyl-formamidine and benzal-diortho-tolyl-thiazolidone were mixed and heated for three hours in an oil bath at a temperature of 160°. No reaction took place. A similar mixture was heated for five hours at a temperature of 200°. No condensation occured. Molar quantities were then mixed and heated for three hours in a sealed tube at a temperature of 185°. The products were recovered apparently unchanged. A similar mixture was then heated for five hours in a sealed tube at a temperature of 210° to 220°. No apparent change took place. The work done showed that in this case, at least,

the benzal group joined to carbon next to a sulfur atom was more difficult to replace than when the original methylene group was adjacent to a CO group.

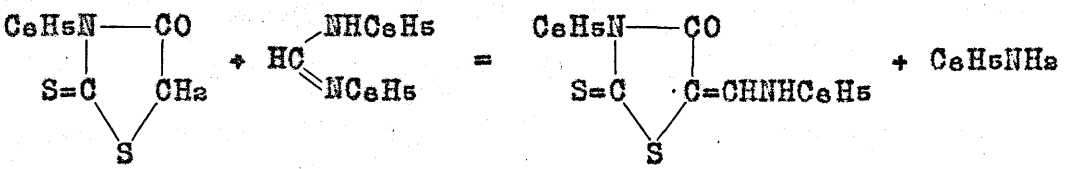
Benzal-Phenyl-Rhodanine with Diphenyl Formamidine.

Benzal rhodanine was prepared after the method of Andreash[14] and Zipser. Molar proportions of 2-thio-3-phenyl-4-keto tetra hydro thiazole and freshly distilled benzaldehyde were mixed and dissolved in glacial acetic acid. A weight of anhydrous sodium acetate equal to the sum of the weights of the benzaldehyde and rhodonine used was added to the solution. The mixture was refluxed gently on an oil bath for about thirty minutes. About three-fourths of the acetic acid was then distilled off. On cooling, an abundance of light yellow needles crystallized from the solution. The crystals were filtered off from the reddish brown mother liquor and washed first with cold alcohol and then with water. The melting point of the purified product was found to be 192°. The melting point observed by Andreash and Zipser[15] was 186°. The reaction is as follows:



Five grams of benzal rhodanine were heated with five grams of diphenyl-formamidine to a temperature of 160° for three hours. No reaction took place. When molar propor-

tions of the two substances were mixed again and heated for three hours to a temperature of 200° in a sealed tube, a reaction took place. The molten mass from the bomb tube was dissolved in alcohol. A residue which was very slightly soluble in hot alcohol was dissolved in hot glacial acetic acid. From the glacial acetic acid, there crystallized about one gram of a lemon yellow product which melted at 248°. In an unpublished thesis done by G. Davis in this laboratory, the annilido-methylene derivative of phenyl rhodanine was obtained. The equation is as follows:

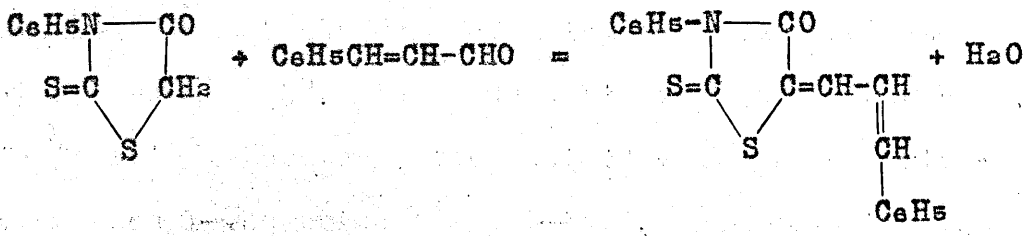


The above annilido-methylene-phenyl-rhodanine melted at 247°. Some of the above product obtained by Davis was mixed with the product obtained by heating benzal-phenyl rhodanine with diphenyl-formamidine. The mixture melted sharply at 247°. It was concluded therefore that the two substances were the same. This reaction shows that the benzal group can be broken with diphenyl-formadine even when S is attached to the original methylene carbon. The difficulty experienced in replacing the benzal group with the annilido-methylene group in the cases of benzal diorthotolyl-thiazolidone and benzal-phenly-rhodanine suggests that the presence of S adjacent to the methylene carbon

tends to make the benzal condensation product more stable.

Cinnamyl-Phenyl-Rhodanine with Diphenyl Formamidine.

Cinnamic aldehyde condenses readily with phenyl rhodanine according to the following equation:



The above reaction was carried out according to the method of Andreash and Zipser[16]. Twelve and five-tenths grams of cinnamic aldehyde and twenty grams of phenyl rhodanine were mixed with an equal weight of anhydrous sodium acetate. Mixture was dissolved in glacial acetic acid and refluxed for thirty minutes. About half the acetic acid was distilled off. On cooling, a light yellow substance crystallized out. The product was washed in alcohol, then in water. It was recrystallized from chloroform. From this solvent, brilliant yellow crystals were obtained. These melted sharply at 223°. Andreash and Zipser report a melting point of 217° for the condensation product. They recrystallized the cinnamyl-phenyl-rhodanine from alcohol. Chloroform was found especially suitable for the preparation of the pure product. In order to make sure that the condensation product obtained was cinnamyl-phenyl-rhod-

anine, a nitrogen determination was made.

Analysis.

Calculated as $C_{18}H_{13}ONS_2$

Theoretical	Found
N = 4.33%	N = 4.29%
	N = 4.36%

It was thought that the cinnamyl group might show a different degree of reactivity when treated with diphenyl-formamidine due to its unsaturated nature. Diphenyl-formamidine was mixed with cinnamyl-phenyl-rhodanine and heated in an oil bath to a temperature of 150°. There seemed to be no reaction, the cinnamyl-phenyl-rhodanine was recovered unchanged. Molar proportions were then placed in a sealed tube and a temperature of 200° was maintained for three hours. As far as could be determined, there was no reaction. Then a similar molar mixture was heated in a bomb tube for five hours at a temperature of 240°. An examination of the products showed that considerable decomposition had occured. Pressure was developed in the bomb tube. The gas formed smelled strongly of H_2S. Attempts to isolate reaction products from the tarry mass were unsuccessful.

Benzal Malonic Ester with
Diphenyl Formamidine.

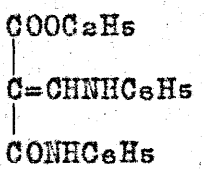
Benzaldehyde and malonic-ethyl-ester were condensed after the method of Knoevenagel[17]. Malonic ethyl ester

(30 grams), freshly distilled benzaldehyde (21 grams), and one gram of piperidine were mixed together. The mixture was allowed to stand two days at room temperature. It was then heated for twelve hours on a water bath. On cooling, ether was added to the mixture which was now a thick oil. The ether solution obtained was thoroughly washed with dilute HCl and water. The ether layer was then separated from the water and anhydrous Na_2SO_4 was added to dry the solution. After standing over night, the ether was distilled off and the benzal malonic ester was distilled under reduced pressure. The product which distilled over at about 200° under a pressure of 20 to 30 m.m. was collected. A thick yellow oil was obtained which would not crystallize. The following equation represents the reaction:

$$\begin{array}{l} COOC_2H_5 \\ | \\ CH_2 \\ | \\ COOC_2H_5 \end{array} + C_6H_5CHO = \begin{array}{l} COOC_2H_5 \\ | \\ C{=}CHC_6H_5 \\ | \\ COOC_2H_5 \end{array} + H_2O$$

Benzal-malonic-ester (24 grams) and diphenyl-formamidine (20 grams) were mixed and heated for three hours at 115° and then for one hour at 150°. The mixture was poured into alcohol and allowed to crystallize. A very white crystalline compound crystallized out which melted at 118°. Practically a theoretical yield was obtained. The melting point agrees with that observed by F. B. Dains[18] for the

monoanilide of annilido-methylene-malonic-ethyl-ester. The formula follows:

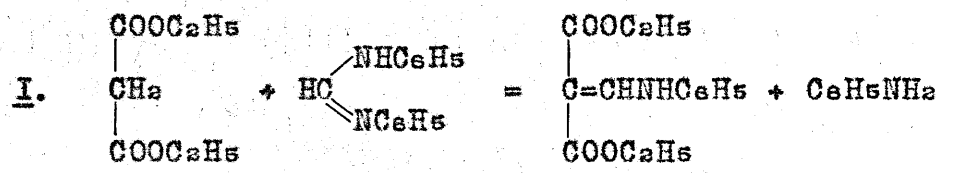


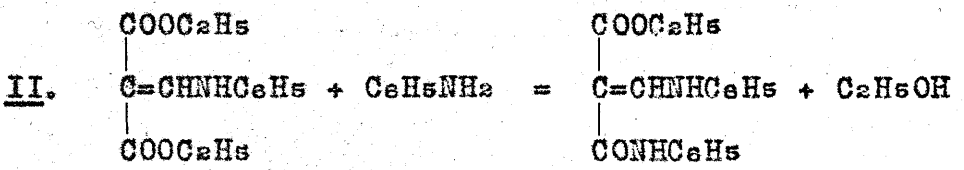
Analysis.

Calculated as $C_{18}H_{18}O_3N_2$

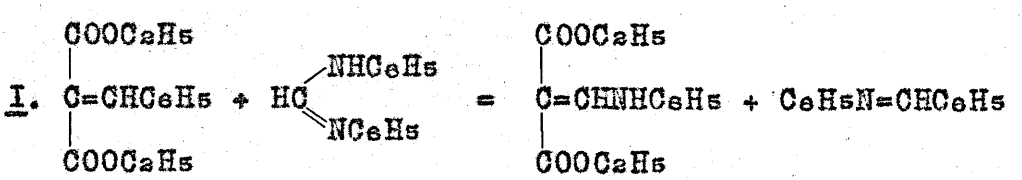
Theory.	Found.
N = 9.03%	N = 8.55%
	N = 9.03%

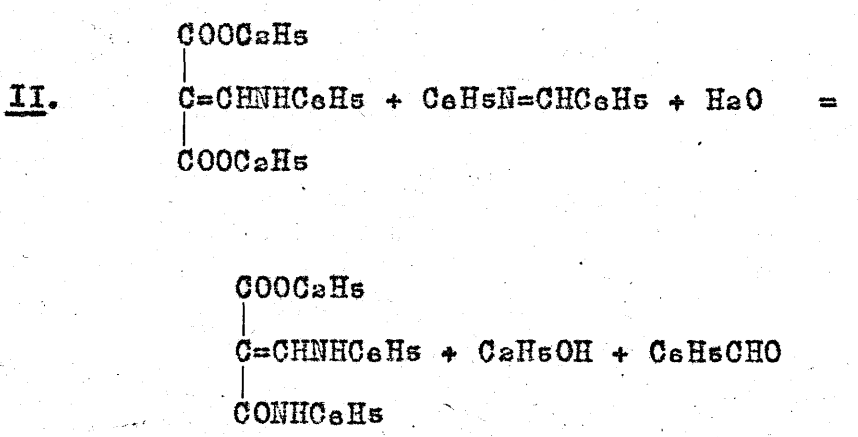
The secondary reaction which results in the formation of a substituted amide from the reaction between the amine and the carbethoxy group often takes place. It seems to depend very largely upon the temperature at which the reaction takes place[19]. When ethyl aceto acetate and diphenyl-formamidine react, it is possible to isolate both the unsubstituted annilido-methylene-ethyl-aceto-acetate and the annilido-methylene-phenyl amide of aceto acetic acid[20]. For these reasons, the reaction between diphenyl formamidine and malonic ester has been thought to proceed in two steps, although the intermediate annilido-methylene-malonic-ester has not yet been isolated. The reactions may be expressed by the following equations:





Since the same final product was obtained when benzal malonic ester was treated with diphenyl formamidine, it is possible that the reaction may be shown by the following equations:





The secondary reaction may have taken place when the mass was extracted with boiling 95% alcohol. Benzal aniline

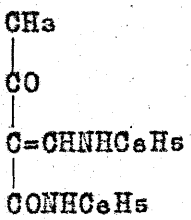
is easily hydrolyzed. Further study is being made on this reaction.

Benzal Aceto-acetic-ester with Diphenyl Formamidine.

The benzal derivative of ethyl aceto acetate was prepared according to the method of L. Claisen and F. E. Matthews[21]. A molecular mixture of aceto acetic ester and benzaldehyde was cooled to 0° and allowed to absorb thirty per cent of its weight of dry HCl gas. During the passage of the gas through the mixture, it takes on a yellowish color and a thick consistency. After standing for several days, two layers appeared. The water layer was removed and the mixture was warmed on a water bath. At the same time, CO_2 was bubbled through the mixture. The HCl was thus removed and the liquid became clear. It was then distilled under reduced pressure. That fraction was collected which distilled over between 180° and 200° at a pressure of 10 m.m. It was a thick light brown oil which did not crystallize. Claisen and Matthews state that after standing about a week, the oil should gradually crystallize. They report the melting point of the crystalline compound as 59 - 60°.

The brown oil so obtained was mixed with diphenylformamidine and heated for three hours at a temperature of 130°. The product was dissolved in alcohol and allowed to stand for about three weeks. A light yellow crystalline

compound was filtered off, washed with alcohol and dried. It melted at 156°. This is the melting point of the anilide of annilido methylene aceto acetic acid[22]. The formula of the anilide of annilido-methylene aceto acetic acid is:



Further study is being made on this reaction.

Benzal Acetophenone with Diphenyl Formamidine.

It has been shown that the CH_3 group next to the CO group in ketones often reacts in much the same manner as the methylene grouping.[23]

It was thought desirable, therefore, to study the reaction between benzal acetophenone and diphenyl formamidine.

Benzal acetophenone was prepared according to the method of Claisen and Cloparede[24]. Molecular proportions of benzaldehyde and acetophenone were mixed and the mixture cooled to approximately -5° in a freezing mixture. While cold, the mixture was saturated with dry HCl gas. After it was thoroughly saturated, the flask was tightly stoppered and allowed to stand in the freezing mixture for twenty-four hours.

The mixture solidified into a brownish yellow cake.

The flask was taken out of the freezing mixture and heated on a water bath for an hour. Nearly all the HCl was thus driven off. The oily layer was separated from the water layer and the oil dissolved in alcohol. On cooling the alcohol in an ice bath, the benzal acetophenone crystallized out in good yield. The best yield obtained was 250 grams from 200 grams of acetophenone. Benzal acetophenone is a light yellow crystalline substance which melts at 58°.

Molar quantities of benzal acetophenone and diphenyl formamidine were mixed and heated in an oil bath for three hours at a temperature of 130°. The molten mixture was poured into alcohol and allowed to crystallize. A product which crystallized in extremely white crystals separated from the alcohol. The substance melted at 168°. It was found to be very slightly soluble in both hot and cold alcohol. It may be recrystallized readily from benzene.

On heating molar proportions of benzal autophenone and diphenyl formamidine in a bomb tube, a somewhat larger yield of the white product was obtained. By these methods of preparation, never more than five to ten per cent of the diphenyl-formamidine reacted. The unchanged diphenyl-formamidine was separated from the reaction product by fractional crystallization. It was expected that the benzal group might be replaced by the annilido methylene group from the diphenyl-formamidine. If the benzal group had

been replaced a compound isomeric with one obtained by Claisen and Fischer[25] should have been obtained. They condensed acetophenone with ethyl formate as follows:

$$C_6H_5COCH_3 + HCOOC_2H_5 = C_6H_5COCH_2-CHO + C_2H_5OH$$

The benzoyl aldehyde was then allowed to react with aniline:

$$C_6H_5CO-CH_2-CHO + C_6H_5NH_2 = C_6H_5CO-CH_2-CH=N-C_6H_5 + H_2O$$

If the benzal group of the benzal acetophenone had been replaced by the anmilido-methylene group from diphenyl-formamidine, the following compound should have been obtained:

$$C_6H_5CO-CH=CHNHC_6H_5$$

Since this compound differs only in the position of the double bond, from the one obtained above by Claisen, it was thought they might be tautomeric. The compound obtained from benzoyl aldehyde with aniline melted at 141°. The compound obtained from diphenyl formadine and benzal acetophenone melted at 168°. A complete analysis showed:

C = 89.00% - 88.94%

H = 6.15% - 6.31%

N = 4.92% - 4.93%

The results of numerous analyses showed no oxygen and gave the empirical formula, $(C_{21}H_{17}N)_n$. A molar weight determination was made by dissolving a known weight of the compound in benzene and determining the lowering of the freezing point of the benzene. The molar weight from

the lowering of the freezing point was found to be 270 to 286°. Since so small an amount of the substance would stay in solution in cold benzene, some difficulty was experienced in getting concordant results. All determinations showed that the grouping $C_{21}H_{17}N$ occured only once in the molecule.

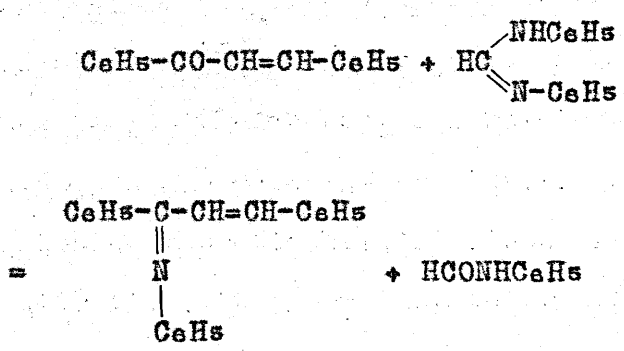
Several grams of the product were refluxed in ten per cent H_2SO_4 solution for three hours. Aniline, benzaldehyde and acetophenone were identified as the hydrolytic products. This showed that the benzal grouping had not been removed.

When dissolved in chloroform, the compound adds bromine very readily. A weighed amount of the product was titrated against a chloroform solution of bromine. If one assumed 283 as the correct molar weight and that the molecule adds one molecule of bromine, .3406 grams of the compound should theoretically add .1925 grams of bromine. From the titration, it was calculated that .3406 grams of the compound actually added .1894 grams of bromine. This was taken as evidence that the compound contained one carbon to carbon double bond.

The chloroform solution of the bromine addition product was evaporated to dryness and the residue dissolved in alcohol. From the alcohol, a light yellow compound containing bromine was obtained which melted at 177°. Study on this bromine addition product is being continued.

In order to determine, if possible, what other products were obtained in the reaction between diphenyl formamidine and acetophenone, the para-brom derivative of diphenyl formamidine was prepared and heated with benzal acetophenone. The products of the reaction were found to be quite difficult to separate but after repeated fractionations a light yellow crystalline compound containing bromine which melted at 117° was isolated. When some of the compound was mixed with para-brom-formanilide, the melting point of the mixture was not lowered.

The evidence points to the following reaction, therefore, between benzal acetophenone and diphenyl formamidine.



Benzal acetophenone is known to add aniline[26]. Tambor and Wilde found that the unsaturated benzal acetophenone would add aniline and similar primary amines in the cold on standing. The addition product was made after the method of Tambor and Wilde. Molar proportions of benzal acetophenone and aniline were dissolved in alcohol. On standing, a white crystalline body crystallized out which

melted at 172°. When the addition product was mixed with the product from the formamidine reaction, the mixture melted slowly between 150° and 160°. The aniline addition product does not add bromine.

Benzal Acetophenone with Aniline.

An attempt was made to prepare the anil of benzal acetophenone by heating benzal acetophenone directly with aniline. Molar proportions of benzal acetophenone and freshly distilled aniline were mixed and heated for four hours at a temperature of 175°. On cooling, there crystallized out of alcohol about a ten per cent yield of the same product as had been obtained from the heating of benzal acetophenone and diphenyl formamidine. A mixture of the two products melted at 168°. In order to determine whether a water removing agent would increase the yield the following method was tried: Twenty grams of benzal acetophenone were mixed with eight and eight-tenths grams of aniline. Twenty grams of anhydrous sodium acetate was added to the mixture, which was then heated for three hours at a temperature of 175°. The molten mixture was then poured into a large volume of water and stirred. An oily liquid settled to the bottom, and was separated from the water. The oil was put in alcohol and heated to boiling. Very soon the alcohol became filled with fine white needles which were very difficultly soluble in the hot alcohol. The crystals were filtered out and recrystal-

lized from benzene. About an 80% yield of the anil was obtained in this way.

Benzal-Acetophenone with Para-chlor-Aniline.

By using the above method para-chlor-aniline and para-toluidine were condensed with benzal-acetophenone. In the case of para-chlor-aniline, a 75% yield of a compound which crystallized in white needles was obtained. This compound melted at 167° and gave a positive test for chlorine. It added bromine readily in chloroform solution. An analysis for chlorine and nitrogen showed the following results:

Analysis.

Calculated as $C_{21}H_{16}ClN$

Theoretical	Found
Cl = 11.16%	Cl = 11.07%, 10.84%
N = 4.41%	N = 4.30%, 4.31%

Benzal Acetophenone with Para-Toluidine.

Para-toluidine was condensed in the same manner with benzal-acetophenone. A similar yield of a white product was obtained. This compound melted at 170°. A nitrogen determination showed the following results:

Analysis.

Calculated as $C_{22}H_{19}N$

Theoretical	Found
N = 4.71%	N = 4.78%
	N = 4.81%

Anil of Benzal Acetophenone.

The unsubstituted anil of acetophenone has been prepared by Claisen[27] and later in a somewhat similar manner by Knovenagel[28]. In each case the ethyl acetal was first prepared by the reaction of acetophenone and orthoformic ester in alcohol. The reaction is as follows:

$$CH_3COC_6H_5 + (C_2H_5O)_2CH\text{-}OC_2H_5 = \begin{matrix} CH_3 \\ | \\ C{=}(OC_2H_5)_2 \\ | \\ C_6H_5 \end{matrix} + HCOOC_2H_5$$

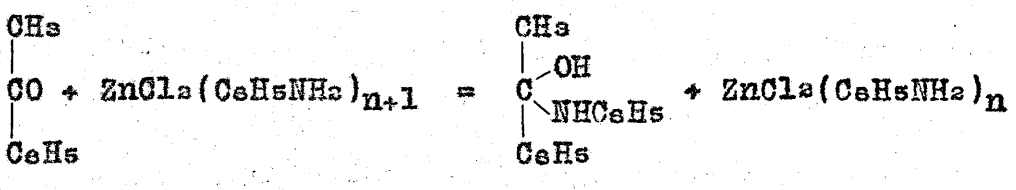
The acetal acetophenone then reacts with aniline thus:

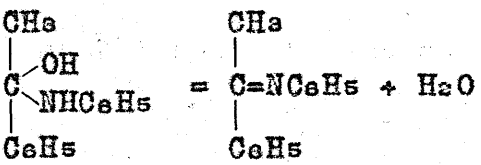
$$\begin{matrix} CH_3 \\ | \\ C(OC_2H_5)_2 \\ | \\ C_6H_5 \end{matrix} + C_6H_5NH_2 = \begin{matrix} CH_3 \\ | \\ C{=}NC_6H_5 \\ | \\ C_6H_5 \end{matrix} + 2C_2H_5OH$$

The unsubstituted anil is a yellow crystalline compound which melts at 41°. G. Reddelien[29] reports the condensation of acetophenone directly with the aid of $ZnCl_2$. He expressed the opinion that the $ZnCl_2(C_6H_5NH_2)_n$ double salt acted as a carrier of aniline. He reports that when he heated acetophenone and aniline with simply $ZnCl_2$, the acetophenone condensed into triphenyl benzene which it does quite readily under other conditions as well. When he first prepared the $ZnCl_2(C_6H_5NH_2)_n$[30] double salt and added it to the mixture of acetophenone and aniline, he obtained the anil of acetophenone. He believed the reaction might be represented thus:

I. $ZnCl_2 + nC_6H_5NH_2 = ZnCl_2(C_6H_5NH_2)_n$

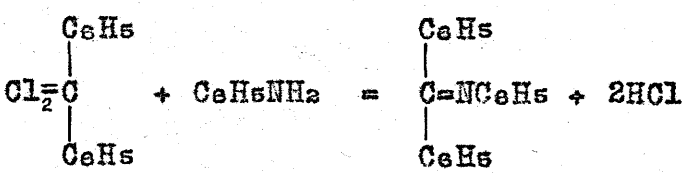
II. $ZnCl_2(C_6H_5NH_2)_n + C_6H_5NH_2 = ZnCl_2(C_6H_5NH_2)_{n+1}$

III.


IV.


Benzophenone and aniline will condense when heated together although only after six to eight hours of heating at a temperature of 240 to 250°. Nagelis[31] prepared the anil of benzophenone by heating benzophenone, aniline, and anhydrous sodium sulfate for twenty hours.[32]

M. Pauly[33] prepared the anil of benzophenone by the reaction of aniline with benzophenone dichloride according to the following equation:



G. Reddelien[34] prepared the anil of benzophenone by heating benzophenone, aniline and dry $ZnCl_2$ to a temperature

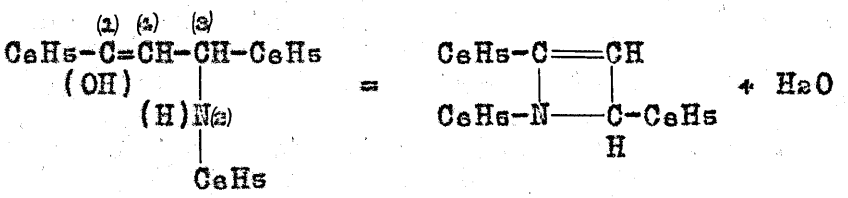
of 160° for thirty minutes. He found that this method gave a good yield and was applicable in the condensation of various aniline derivatives with benzophenone. He condensed in this way ortho, meta, and para-toluidine, amino phenol, and dimethyl-para-phenylene-diamine.

I. Moses[35] working with Knoevenagel prepared the anil of benzophenone by heating ten grams of aniline, seven and five-tenths of benzophenone and one-tenth gram of iodine.

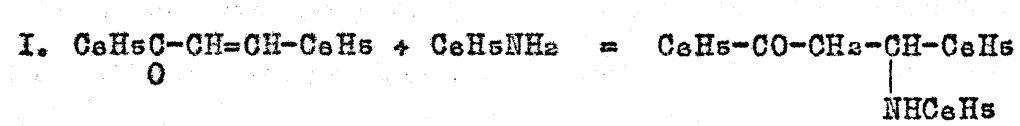
It appears, therefore, from the work done, that the anil of benzophenone is much more readily prepared than the anil of acetophenone. The anil of benzal-acetophenone is not found in the literature. The proof is not considered conclusive, as yet, that the compound $C_{21}H_{19}N$, which was obtained, first, from the reaction of benzal-acetophenone and diphenyl-formamidine is the anil of benzal acetophenone. The fact that the same product has been prepared by heating benzal acetophenone, aniline and anhydrous sodium acetate suggests that the aniline addition product may first be formed thus:

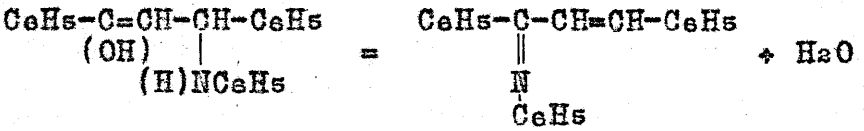
$$C_6H_5-\underset{\underset{O}{\|}}{C}-CH=CH-C_6H_5 + C_6H_5NH_2 = C_6H_5\underset{\underset{O}{\|}}{C}-CH_2-\underset{\underset{C_6H_5}{|}}{\overset{\overset{NH}{|}}{CH}}-C_6H_5$$

This addition product may rearrange and lose water thus:



A ring compound of the above type is not known, however. It would contain a tertiary nitrogen which should resist hydrolysis. The compound obtained hydrolyzes very easily into aniline, benzaldehyde and acetophenone. It is possible that the aniline group after addition shifts into the anil formation as follows:

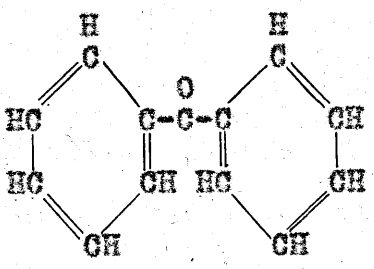


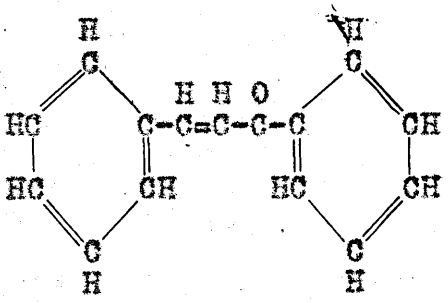


Further work is planned to determine the constitution of the product and the steps in the reaction. At present, it appears most probable that the compound is the anil of benzal-acetophenone.

The facts observed would indicate that the reactivity of the CO group had been considerably increased by the addition of the benzal grouping. The negative nature of the double bond has apparently caused the CO grouping in benzal acetophenone to resemble more closely the CO grouping in benzophenone. A comparison of their formuli suggests

that this might be the case:

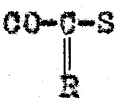




It will be observed that the CO group is in each case joined to carbon which is doubly bound to an adjacent carbon.

SUMMARY AND CONCLUSION.

Since the reactions studied have been comparatively few, any general conclusions are impossible. Work is being continued in order to determine what general laws govern the breaking of the carbon to carbon double bond. The study thus far shows that a doubly bound carbon group may be replaced by other groups without disruption of the molecules in case the methylene group is between two CO groups. This was found to be the case with methyl-phenyl-pyrazolone, malonic-ester, and aceto-acetic ester. The group



seems to be more stable. It was found impossible to replace the benzal group in diortho-tolyl-thiazolidone. However, after long heating at 200° in a bomb tube, the benzal group in benzal phenyl rhodanine was replaced in small yield by the

anilido-methylene group from diphenyl-formamidine. In the case of benzal-acetophenone, the double bond was not broken but its presence seemed to materially increase the ease with which the CO group condensed with aryl primary amines.

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